REMARKS

Applicant thanks the Examiner for removing the finality of the previous Office Action and for considering applicant's arguments in response to his request for continued examination.

Claim Amendments

Applicant has amended claim 3 to recite a method of making solamargine comprising the reaction of solasodine with tetra-O-benzoyl-α-D-glucopyranosyl bromide, tetra-O-acetyl-α-D-glucopyranosyl bromide or tetra-O-pivaloyl-α-D-glucopyranosyl bromide; followed by optionally de-protecting the obtained glycoside to yield a compound of the formula V and reesterification of the most reactive hydroxyl groups (OH-3 and OH-6) to yield a compound of the formula IIa. Support for this amendment may be found, *inter alia*, in claim 2, as originally filed.

Applicant makes this amendment expressly without waiver of his right to file for and to obtain claims directed to the canceled subject matter in applications claiming priority and benefit herefrom.

This amendment does not constitute new matter. Its entry is requested. Upon entry of the amendments, claims 1-3, 5-7, and 9 will be pending in this application.

Obviousness-Type Double Patenting

Claims 1-3, 5-7, and 9 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being allegedly unpatentable over the claims of

co-pending United States patent application 10/555,038 in view of Cham et al. (U.S. Patent 5,958,770) ("***Cham***)" and Schmidt et al. (U.S. Patent 6,242,583) ("***Schmidt***"). Applicant requests that this rejection be held in abeyance until allowable subject matter is found in the instant application and the '038 application. Applicant will then respond to the obviousness-type double patenting rejection in the appropriate way, *i.e.*, by argument or by the filing of the appropriate Terminal Disclaimer.

35 U.S.C. §103(a): Obviousness

(i) Claim 1

Claim 1 stands rejected under 35 U.S.C. §103(a) as allegedly obvious over ***Cham*** in view of ***Schmidt***. Specifically, the Examiner contends that ***Cham*** discloses a glucose conjugate of solasodine, wherein the hydroxy groups are substituted by acetyl groups and that ***Schmidt*** teaches the use of benzoyl and pivaloyl groups in sugar synthesis. The Examiner further argues that despite ***Cham's*** teaching of solasonine and solamargine derivatives' role in the control of cellular function, the skilled artisan would be motivated to synthesize additional non-natural derivatives of solasonine and solamargine. Applicant traverses.

The control of cellular function is a tightly regulated process dependent on specific ligand-receptor interactions. It is also known in the art that the composition of the carbohydrate moieties of steroidal alkaloids can alter the binding specificity to steroid receptors. *See e.g.,* Chang LC et al., BBRC (1998) vol. 242(1): 21-25 (copy enclosed). As such, the skilled artisan would not be motivated to alter the composition of the glucose conjugate of solasodine taught to be biologically active in the context of cellular function by ***Cham***. In addition, even if such change were suggested (which it is not), the skilled artisan would have no expectation that

benzoyl or pivaloyl substituted glucose conjugates of solasodine would retain that biological activity. Indeed, nothing in ***Cham*** or ***Schmidt*** teaches or suggests that benzoyl or pivaloyl substituted glucose conjugates of solasodine would be biologically active regulators of cellular function. Therefore, the benzoyl and pivaloyl substituted glucose conjugates of solasodine are not obvious over ***Cham*** in view of ***Schmidt***, even in the context of cellular function. Therefore, these documents certainly do not render the pending claims –directed to conjugate intermediates for the synthesis of solamargine and solasonine—obvious. Applicant requests reconsideration and withdrawal of this obviousness rejection.

(ii) Claims 2 and 5-7

Claims 2 and 5-7 stand rejected under 35 U.S.C. §103(a) as allegedly obvious over ***Cham*** in view of Holick (U.S. Patent No. 5,612,317)("***Holick***") and in view of ***Schmidt***. Specifically, the Examiner argues that ***Cham*** discloses glucose conjugates of solasodine, ***Holick*** teaches a supposedly conventional method for glycosylating an analogous steroid derivative by reacting a steroid with a protected sugar donor, and ***Schmidt*** discloses the use of acetyl, benzoyl, and pivaloyl protecting groups in sugar synthesis. Applicant traverses.

The hydroxy group of solasodine is relatively unreactive. Indeed, the specification discloses that solasodine is not compatible with the conventional steroid glycosylation technique whereby solasodine is treated with tetrabenzoyl α-D-glucopyranosyl trichloroacetimidate and trimethyl-silyl triflate or trifluroride etherate. *See e.g.*, page 3, lines 3-12. As such, only specific glycopyranosyl donors may be used in the glycosylation of solasodine. ***Holick*** refers to conventional steroid glycosylation. It does not recognize that only specific donors are useful in the glycosylation of solasodine (and ***Schmidt*** does not remedy that

defect). Claims 2 and 5-7, by contrast, recite stereospecific β-glycosylation of solasodine requiring specific glucopyranosyl donors. Further, the steroid of ***Holick*** is not analogous to solasodine. *See e.g.*, the substitution pattern on the five member ring. ***Schimdt*** does not remedy this defect. As such, claims 2 and 5-7 are not obvious over ***Cham*** in view of ***Holick*** and in view of ***Schmidt***. Applicant requests reconsideration and withdrawal of this obviousness rejection.

(iii) Claims 3 and 9

Claims 3 and 9 stand rejected under 35 U.S.C. §103(a) as allegedly obvious over ***Cham*** in view of Ohira et al. (U.S. Patent No. 6,084,081)("***Ohira***"). Specifically, the Examiner argues that ***Cham*** discloses solamargine and glucose-solasodine conjugates and that ***Ohira*** discloses glycosylation of a sugar moiety.

Applicant has amended claim 3, and, thus, dependent claim 9 to recite the synthesis of solamargine from solasodine. As discussed above, the glycosylation of solasodine is not obvious in light of the prior art. The hydroxy group of solasodine is relatively unreactive. Indeed, the specification discloses that solasodine is not compatible with the conventional steroid glycosylation technique whereby solasodine is treated with tetrabenzoyl α-D-glucopyranosyl trichloroacetimidate and trimethyl-silyl triflate or trifluroride etherate. *See e.g.*, page 3, lines 3-12. As such, only specific glycopyranosyl donors may be used in the glycosylation of solasodine. ***Ohira*** does not teach the stereospecific β-glycosylation of solasodine requiring specific glucopyranosyl donors. The amended claims, by contrast, recite stereospecific β-glycosylation of solasodine requiring specific glucopyranosyl donors followed by subsequent deprotection, reesterification, and glycosylation. As such, the amended claims are not obvious over ***Cham*** in view of ***Ohira***. Applicant requests reconsideration and withdrawal of this obviousness rejection.

CONCLUSION

Applicants request favorable consideration and allowance of claims 1-3, 5-7, and 9.

Respectfully submitted,

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